disease prevention news

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Nonpolio Enteroviruses - The Summer Headache

An estimated 10 to15 million cases of nonpolio enteroviral infections (NPEVs) occur annually in the United States, with the highest incidence occurring in late summer and early fall. The 67 recognized NPEV serotypes produce a variety of illnesses. More than 90% of persons infected are asymptomatic or have only mild febrile illnesses. The 10% who have more serious symptoms are at risk of developing rare complications. For this reason, NPEVs must be differentiated from the common treatable bacterial infections with similar presentations. This article summarizes the classification of enteroviruses and the mild NPEV syndromes. Central Nervous System syndromes are described in more depth. The companion article profiles TDH laboratory results on NPEV testing done in 1996.*

Enteroviruses are categorized as follows: polioviruses; coxsackie groups A and B; echoviruses; and the numbered enteroviruses. Poliomyelitis is no longer a major health threat in the developed world. Vaccination with oral polio vaccine (OPV), a live attenuated virus, is the primary cause of the 5-10 annual cases of polio in the US (risk: 1 case per 2.6 million doses distributed). Administration of inactivated polio vaccine (IPV), followed by OPV, has been shown to reduce the risk of vaccine-associated polio while retaining the benefit of the live attenuated virus.

The nonpolio enteroviruses, which comprise the other three categories, can cause infections that vary greatly in presentation and severity. Patients with NPEV infection may present with a fever and rash, herpangina, pleurodynia, mild respiratory or gastrointestinal illness, conjunctivitis, or central nervous system (CNS) symptoms. CNS diseases caused by NPEVs range from aseptic meningitis and encephalitis to Guillan-Barré type syndromes and paralysis.

Non-CNS Syndromes

Coxsackie virus and echovirus infections present as multiple syndromes. **Herpangina**, caused by coxsackie group A viruses, begins with a sudden onset of fever followed by vomiting, myalgia, and headache. These symptoms usually do not persist but often are followed by a sore throat. From 1 to 2 hours later punctate pharyngeal macules develop and progress to papules that vesiculate and ulcerate. **Acute lymphonodular pharyngitis**, also caused by coxsackie group A viruses, has a similar picture, but the mucosal enanthem does not vesiculate and ulcerate.

Pleurodynia is most commonly caused by viruses in the coxsackie B group. This illness begins with an abrupt onset of spasmodic pain, usually located over the lower rib cage or upper abdomen. This infection inflames the muscle, rather than the pleura or peritoneum, resulting in paroxysmal pain lasting 4 to 6 days, with possible later recurrences. Aseptic meningitis has been seen in 3 to 6% of patients 4 to 6 days after the onset of the paroxysmal pain. **Diabetes** also has been associated with coxsackie group B.

Myopericarditis can be caused by coxsackie virus types A-4 and A-16, all coxsackie group B viruses, and echoviruses 9 and 22. In two-thirds of cases, onset of cardiac disease is preceded by an upper respiratory illness and

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commonly followed by dyspnea, chest pain, fever, and malaise. Evidence of myocarditis and pericarditis is seen on the electrocardiogram. Although convalescence may be prolonged, most patients recover uneventfully. The fatality rate is low: 0-4%.

Febrile illness with or without respiratory symptoms and **diarrhea** are also frequent syndromes associated with coxsackie virus and echovirus infections. Other, more complicated syndromes associated with both these groups include **Reye syndrome** and **hemolytic uremic syndrome**.

Acute hemorrhagic conjunctivitis is usually caused by enterovirus 71. The characteristic subconjunctival hemorrhages and swelling of the eyelids persist about a week.

Most of the serotypes in each NPEV category can cause CNS syndromes

CNS Syndromes

Most of the serotypes in each NPEV category can cause CNS syndromes, which include aseptic meningitis, encephalitis, and paralysis. NPEVs account for 80 to 92% of aseptic meningitis agents. An estimated 75,000 cases occur in the US annually. The number of encephalitis cases caused by NPEV infections is difficult to estimate because these pathogens are hard to distinguish from others also associated with encephalitis. For instance, *Herpes simplex* virus, the most commonly identified etiologic agent of encephalitis in the US, accounts for only 10% of encephalitis cases.

The following sections describe the clinical presentation, pathogenesis, diagnostic techniques and treatment for CNS diseases caused by NPEVs. Clinical presentation of NPEV infections of the CNS varies, based primarily on the age and immune status of the patient.

Clinical Presentation. A diagnosis of **aseptic meningitis** is made when a patient presents with symptoms consistent with meningeal infection, but no bacterial agent can be identified. The course of illness is usually mild. Older children and adults typically present with headache associated with the usual symptoms seen in mild NPEV syndromes: vomiting, anorexia, rash, cough, pharyngitis, diarrhea, and myalgias. Photophobia frequently occurs as well. Symptoms typically last only 5 to 7 days and may be relieved by the lumbar puncture used to diagnose the illness. Young children may have febrile seizures. Late neurocognitive sequelae in children have been postulated, but the largest controlled study did not show this result.

Neonates acquiring NPEV infections in the first few days of life are at greatest risk of dying. Several days after the birth, they often develop a biphasic fever and nonspecific symptoms followed by meningeal signs. While illness can include myocarditis and/or hepatitis, 75% of patients with proven EV infections have signs and symptoms of meningitis or meningoencephalitis. The neurologic picture may progress to encephalitis although hepatitis or sepsis is the usual cause of death.

When additional neurologic signs are present, a diagnosis of **encephalitis** may be more appropriate. NPEV encephalitis is likely to result in devastating consequences. Symptoms and signs are usually consistent with general neurologic depression: drowsiness, personality changes, seizures, and coma may all be manifested.

The differential diagnosis includes arbovirus infections, LCM, and mumps. Other considerations include toxic encephalopathies and postinfectious

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encephalitis. In individuals with immune deficiencies such as agammaglobu-linemia, chronic meningitis or meningoencephalitis can occur. Enterovirus 71 infection can present as an asymmetric flaccid **paralysis**, in much the same manner as classic polio.

Pathogenesis. Most of the understanding of the pathogenesis of the enteroviruses is from work done on polioviruses. The fecal-oral route is the primary route of infection. NPEVs travel to the intestine and presumably bind to enterocytes. The virus particles then travel to Peyer's patches where they replicate. Depending upon the amount of replication, a major or minor viremia ensues, seeding other organs, including the CNS. How the virus crosses the blood-brain barrier is still not clearly understood. Once in the CNS, the NPEV attaches to a cell receptor site and begins replicating. Within 6 hours of infection, protein production in the host cell is shut down, replaced completely with virus production. Infected tissues are inflamed and necrotic; tissue damage correlates to virus titer. Exposure to cold, malnutrition, pregnancy, and immunosuppression with steroids or radiation increases the severity of disease in experimental animals.

New Diagnostic Techniques. Current laboratory diagnostic methods permit identification of specific viral pathogens in 55 to70% of aseptic meningitis cases. Cell culture remains the gold standard for detecting NPEV in CNS fluid. Available through major laboratories, testing is complete 14 days after set up. A rapid diagnostic assay would provide optimal results and allow for early differentiation between aseptic meningitis and bacterial meningitis. However, the large number of serotypes among which the assay must distinguish has hampered development of this diagnostic tool. DNA and RNA probes have been developed but do not permit clinical detection of virions in the CNS. The polymerase chain reaction (PCR) test may prove to be the most useful tool for diagnosing CNS infections. Several clinical studies using PCR in comparison to DNA/RNA probes and viral culture have found PCR to be 100% sensitive and specific. PCR has already been adapted to colorimetric techniques and, once available, should provide rapid diagnosis of NPEV infections.

The PCR test may prove to be the most useful tool for diagnosing CNS infections.

Treatment. Supportive therapy is the current treatment. Although some experimental antivirals have been tested, lack of capability to diagnose infection has prevented clinical trials from being done. With the advent of PCR testing, new treatment trials are beginning.

For further information contact Dr. Kate Hendricks at (512) 458-7676.

References

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Adapted from *Non Polio Enteroviruses - The Summer Headache*, written by Risa Webb, MD, DTMH, Infectious Diseases Medical Consultant, MSDH, of the Mississippi State Department of Health and published in the August 1996 issue of Mississippi Morbidity Report.

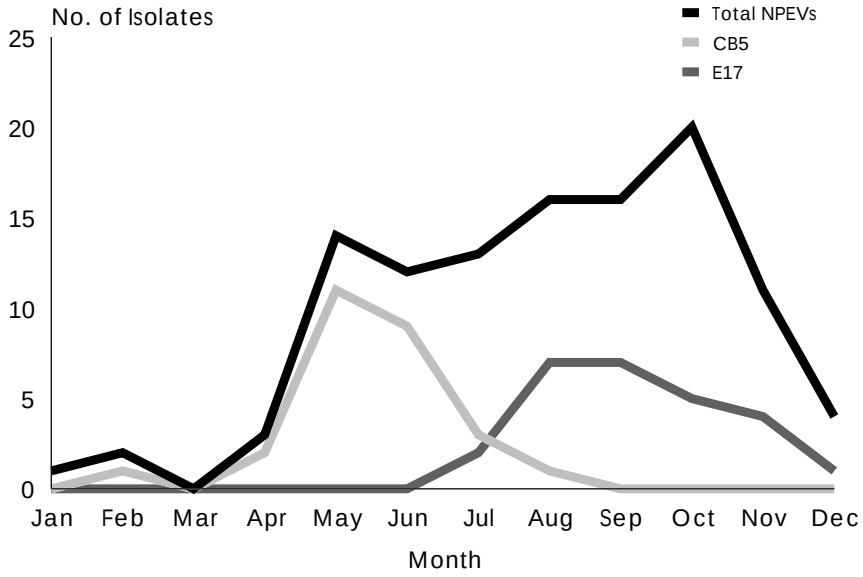
* Four of the 71 viruses previously recognized as distinct enterovirus serotypes have been reclassified.

Nonpolio Enteroviruses - TDH Laboratory Testing in 1996

The enteroviruses are a group of 67* recognized virus serotypes including polioviruses, coxsackie A and B viruses, echoviruses, and the numbered enteroviruses. Although poliovirus vaccine strains are frequently isolated from young children, they will not be addressed in this report because polioviruses isolated in 1996 have limited epidemiological significance.

Nonpolio enteroviruses (NPEVs) are found worldwide. In Texas' temperate climate, NPEVs are isolated primarily in summer and fall. The mode of transmission is mainly by the fecal-oral route. NPEVs can be isolated from feces, pharyngeal specimens, spinal fluids, blood, urine, vesicle fluid, and conjunctiva. Virus can be recovered from the pharynx only during the first week of illness, but from fecal specimens for at least 3 to 5 weeks. Therefore, the patient can be a source of infection long after the symptoms have resolved. The incubation period for NPEV infections is usually 1 to 2 weeks, but varies from 2 to 35 days.

Figure 1. Isolates by Month of Specimen Collection



The Viral Isolation Laboratory uses a combination of cell cultures to isolate viruses. The isolates can be identified by serum neutralization or immunofluorescence. Immunofluorescence is used to identify 14 of the NPEVs, including coxsackie virus types A9 and A24; coxsackie virus types B1 through B6; echovirus types 6, 9, 11, and 30; and enterovirus types 70 and 71. For these viruses, the time necessary for serotype identification is generally 2 to 4 days from receipt of the specimen and is primarily dependent upon the speed with which the isolate grows in cell culture. For the NPEVs that must be identified by a serum neutralization test, the time necessary for serotype identification is generally several weeks, again dependent on the isolate's growth pattern.

The laboratory recovered a total of 120 NPEVs from 115 patients whose specimens were collected during 1996. Five patients had the same NPEV recovered from multiple specimens. The specimens were submitted from the following Texas counties: Bell, Brazos, Dallas, El Paso, Galveston, Harris, Lubbock, Navarro, Nueces, Potter, Tarrant, and Travis.

Dates of collection were available for 112 of the 120 specimens that yielded NPEVs. NPEVs were recovered from specimens collected during every month of 1996, except March (Figure 1). Of the 120 specimens that yielded a NPEV, 102 (85%) were collected in the seven-month period from May through November 1996.

Ages were available for 84 of the 115 patients: 50%, younger than 6 months; 20%, 6 months to 3 years; 17%, 4 to 9 years; 8%, 10 to 24 years; and 5%, older than 25 years. Sex was indicated for 94 patients: 61 (64.9%) were male, and 33 (35.1%) were female.

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Table 1. Patients with NPEV Isolates

Virus	No.	%
Coxsackie A9	7	6.1
Coxsackie B2	3	2.6
Coxsackie B3	1	0.9
Coxsackie B4	4	3.5
Coxsackie B5	28	24.3
Echovirus 2	1	0.9
Echovirus 4	1	0.9
Echovirus 6	14	12.2
Echovirus 7	1	0.9
Echovirus 11	6	5.2
Echovirus 14	2	1.7
Echovirus 16	3	2.6
Echovirus 17	26	22.6
Echovirus 18	2	1.7
Echovirus 21	5	4.3
Echovirus 22	8	6.9
Echovirus 25	1	0.9
Echovirus 30	1	0.9
Enterovirus 71	1	0.9
Total	**115**	**100.0**

Nineteen different NPEVs were isolated from patients in 1996 (Table 1). Coxsackie viruses were isolated from 43 patients, echoviruses were isolated from 71 patients, and enterovirus type 71 was isolated from 1 patient. Two specimens from 1 patient yielded coxsackie B virus type 4 isolates and 2 specimens from each of 4 patients yielded echovirus type 17 isolates. Coxsackie B virus type 5 (CB5) and echovirus type 17 (E17) were isolated most frequently. CB5 was recovered from the specimens of 28 patients and E17 was recovered from 30 specimens collected from 26 patients.

CB5 and E17 isolates formed two peaks of viral activity (Figure 1). Dates of collection were available for 27 of the 28 CB5 positive specimens and 26 of the 30 E17 positive specimens. The CB5 peak occurred during the first half of the year and the E17 peak occurred during the second half of the year. Only 4 CB5 isolates were recovered from specimens collected after July 1, 1996. No E17 isolates were recovered from specimens collected prior to July 1, 1996.

Specimen source for the most commonly isolated NPEVs is listed in Table 2. CB5 was isolated from 28 specimens, echovirus type 6 (E6) was isolated from 14 specimens, and E17 was isolated from 30 specimens collected from 26 patients. More CB5 isolates were recovered from respiratory specimens than from CSF or stool specimens; whereas, more E6 and E17 isolates were recovered from CSF than from stool or respiratory specimens.

Specimens for isolation of enteroviruses can be sent to the Texas Department of Health in Austin. Specimens should be collected as early in the illness as possible and sent in immediately. Specimens can be stored and shipped at 4° C (wet ice or cold packs) if the time period from specimen collection to arrival at TDH will be less than or equal to 72 hours (3 days). If the time period from specimen collection to arrival at TDH will be greater than 72 hours, freeze the specimens at -70° C or with dry ice and ship on dry ice. A completed G-1 form should accompany each specimen.

Table 2. Source of Common NPEVs

	Source			
Virus	**CSF**	**Stool**	**Respiratory**	**Other***
Coxsackie B5	6	7	11	4
Echovirus 6	9	3	1	1
Echovirus 17	17	9	3	1
Total	**32**	**19**	**15**	**6**

*oral, pericardial, genital, blood

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Prepared by Mary Ann Patterson, TDH Medical Virology Branch.

* Four of the 71 viruses previously recognized as distinct enterovirus serotypes have been reclassified.

New Legislation Regarding Spousal Notification of Possible HIV Exposure

The Ryan White CARE Act Amendments of 1996 require states to make a good faith effort to notify a known HIV-infected person's spouse that he or she may have been exposed to HIV and may benefit from counseling and testing.

As of April 1, 1997, TDH will provide information on spousal notification requirements and procedures to all individuals reporting cases of HIV infection and AIDS. The procedures require that a person diagnosed with HIV infection or AIDS be

- asked if they have, or have had, a spouse, and
- informed that s/he should notify their spouse or former spouse(s) of the potential exposure to HIV.

The procedures will outline what services are available for reporting individuals who request assistance with the notification process. Failure to follow the procedures will jeopardize Ryan White CARE Act funds for Texas.

In this legislation, a spouse is defined as "any individual who is the marriage partner of an HIV-infected patient, or who has been the marriage partner of that patient at any time within the 10-year period prior to the diagnosis of HIV infection." In Texas, if two people consider themselves married and represent themselves as such, they should be considered married for notification purposes. Reasonable efforts must be made to determine if each patient with HIV infection intends to notify his or her spouse/former spouse(s) or agrees to have a health department disease intervention specialist (DIS) notify them. Combinations of the two notification methods are acceptable. For example, a person may inform her/his current spouse and choose DIS notification for the former spouse(s), especially if that person lives out of town.

Call the HIV/STD Training and Public Education Branch at (512) 490-2535 to receive a fact sheet on the new spousal notification requirements.

CDC Funding for Blood Safety Promotion and Joint Disease Reduction

The Hematologic Diseases Branch, Division of AIDS, STD, and TB Laboratory Research, is providing funding to 144 hospital-based hemophilia treatment centers (HTCs) to participate in a focused program to prevent the complications of bleeding disorders. During the first few years of the program, blood product safety and joint disease reduction will be priorities.

The funding provides partial reimbursement for preventive services at the HTCs that are not covered by insurance, such as the salaries of nurse coordinators, social workers, and other staff. Maintaining this infrastructure for the HTCs will provide CDC with an established network for gathering information needed to plan methods for preventing complications of hemophilia, as well as a mechanism for researching and carrying out preventive treatment.

One of the first steps toward building this prevention system is the implementation of a nationwide system to gather data on persons with hereditary bleeding disorders. This system will monitor the safety of the blood supply and track the health of persons with bleeding disor-

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ders, including their viral infection status, joint disease, level of functional limitations, and type and source of care.

Each patient seen at an HTC will have access to free blood testing provided by CDC funding to determine the occurrence of bloodborne infections. CDC will maintain the blood samples in a national repository for further testing if new infections are suspected in the blood supply or if new tests are developed. The repository will provide a means for rapidly tracing and identifying threats to the blood supply affecting recipients of blood products.

Acute illnesses will be reported to CDC so staff can investigate potential infection sources and identify outbreaks of infectious diseases that result from treatment with blood products. Morbidity and mortality data collected from the system will provide researchers and HTC staff with the information needed to evaluate patterns of complications and assess the effectiveness of prevention activities.

This program is also promoting a close working relationship between consumers and providers to achieve common prevention goals. The closer ties between the consumer-based organizations and HTCs will create opportunities for consumers to have input into treatment center prevention programs.

Reprinted from CDC / NCID. Focus on AIDS, STD, and TB Laboratory Research. Focus 1997; 6(2):3-4.

Advances in Needlestick Prevention

Two new studies indicate that the use of safer needle designs can reduce the risk of needlestick injuries among health care workers.

By reducing the risk of needlestick injuries, the safer needles will in turn reduce the risk of infection with bloodborne pathogens such as the human immunodeficiency virus (HIV) and hepatitis B and C viruses.

The two studies were conducted by NCID's Hospital Infections Program (HIP), in collaboration with eight hospitals in three US cities. Results were published in the Jan. 17, 1997, issue of the *MMWR*.

One study reported on the use of blunt suture needles during gynecologic surgery and the other on the use of safer needles for drawing blood (one of the most common medical procedures).

The studies found that blunt suture needles may reduce the likelihood of a needlestick during surgery by as much as 86% and that safer needles for drawing blood may reduce needlesticks to health care workers by 27% to 76%.

Of the 51 health care workers with occupationally acquired HIV infection in the United States, 45 are known to have been infected through a needlestick. Annually, several hundred workers are believed to contract HBV in this way.

The studies found that the use of safer needles did not lessen the quality of patient care. Further, the safer needles were generally accepted by health care workers.

The Public Health Service is evaluating the results of the studies, along with other information, in assessing the need for recommendations for safer needles and other instruments in the health care setting.

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Elevated Mercury Levels In King Mackerel - Advisory Continues

On June 10 of this year the Texas Department of Health (TDH) issued an advisory limiting the consumption of king mackerel caught in all waters off the Texas Coast. The advisory does not apply to canned mackerel. Similar advisories have been issued in Florida, Alabama, and Mississippi.

Although mercury content in the coastal waters of Texas is negligible, elevated levels of mercury in the edible tissue of king mackerel caught in these waters have been laboratory confirmed. Recommendations for consumption are as follows:

King Mackerel 43 in. or longer	DO NOT EAT
King Mackerel 37-43 in.	Adults: Eat only one 8-oz serving per week. Children: Eat only one 8-oz serving per month. Women who are, or can become pregnant: Eat only one 8-oz serving per month.
King Mackerel under 37 in. long	(No Restriction)

Young children and infants exposed prenatally are at highest risk of harmful effects to the central nervous system.

For further information regarding this advisory, contact Michael Ordner, Survey Branch Chief of the TDH Seafood Safety Division, at (512) 519-0215. For medical information concerning mercury poisoning, contact Richard Beauchamp, MD, of the TDH Bureau of Epidemiology, at (512) 458-7268.